Mechanistic Modelling of Fluid Bed Granulation Process: Improved Design of Experiment via Degree of Wetness

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ABSTRACT

Fluid bed granulation (FBG) is extensively used in pharmaceutical industry to improve the granule attributes (e.g. size distribution, density and porosity, and granule strength) as well as the finished product attributes (e.g. content uniformity, dissolution/integration, and moisture content) [1]. Fluid bed granulation processes are associated with various phenomena including: i) evaporation of freely-flowing droplet; ii) deposition of droplet on the particle surface; iii) particle drying; and vi) agglomeration of wet particles. The strong coupling of heat and mass transfer [2] influences the performance of an FBG. Therefore, as the contribution of the involved phenomena cannot be readily measured via experiments, exploiting numerical tools can be of high advantage to acquire a better understanding of the FBG performance. Previous numerical studies focused on developing agglomeration model based on empirical kernels [3] or a-priori knowledge of bed properties such as compartment size and circulation rate [4] .

Present study aims on predicting the performance of a fluid bed granulator (FBG) through a numerical and experimental study. In detail, a mechanistic, validated compartment model was developed to predict the temporal evolution of the granule attributes during the granulation process. To realize it, a set of population balance and heat and mass conservation equations were extended and solved in gPROMS platform [5]. Experimental data revealed that the observed granule attributes is highly governed by the operating conditions such as temperature, spray rate and binder concentration. It was also observed that the final granule size can connected to the final granule Loss on Drying (LoD). Analysing the experimental data also demonstrated that the effect of operating conditions can be lumped to the introduced parameters called Degree of Wetness (DoW). This facilitated the development of the correlations for the model parameters associated with agglomeration and drying models. The fidelity of the developed FBG model and correlations were validated for a set of operating conditions. Subsequently, aimed at cutting the cost associated with the experimental run, a DoW-based approach was developed to reduce the number of batches required for the design of experiment (DoE) and correlation development. Comparing the predicted granule attributes with the observed one proves the reliability of the proposed DoW-based approach as well as the developed FBG model for more efficient DoE, which can be used for more efficient design and optimization of FBG process.

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